Improving MAnagement in GastroEnterology

Coeliac Disease

Richard Stevens

Pathogenesis of Coeliac Disease

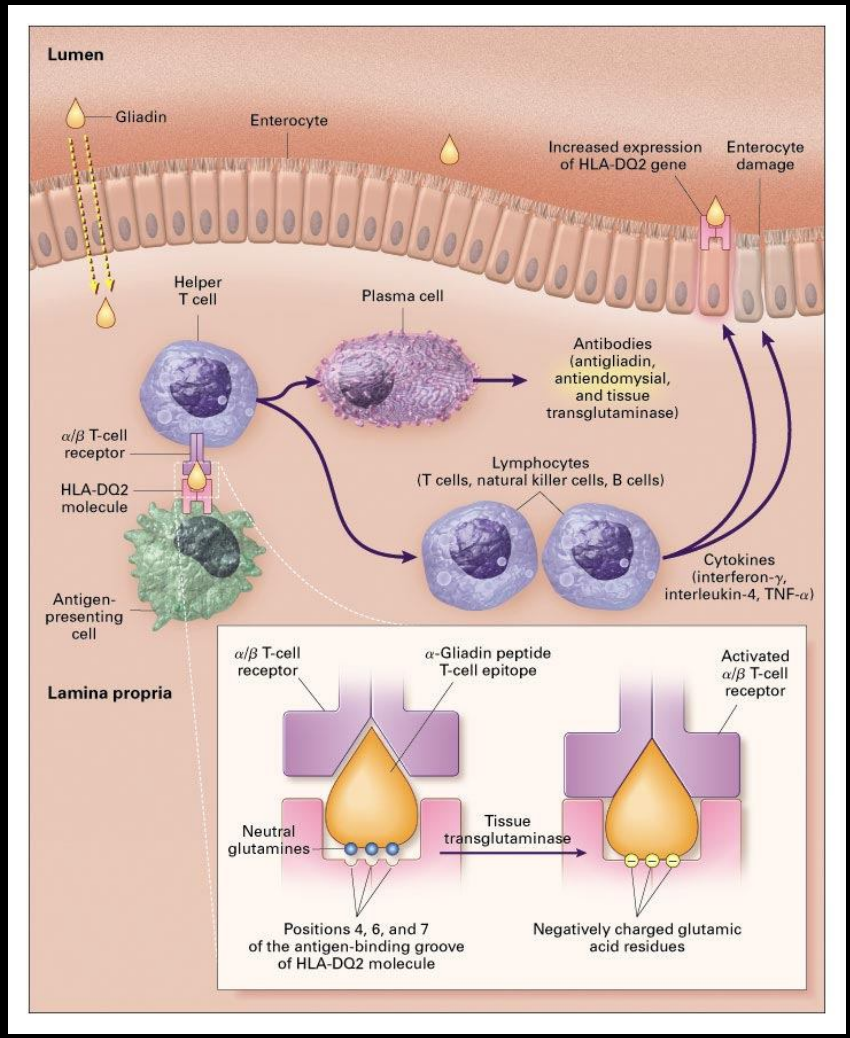
- “Allergy to gluten”

Or …

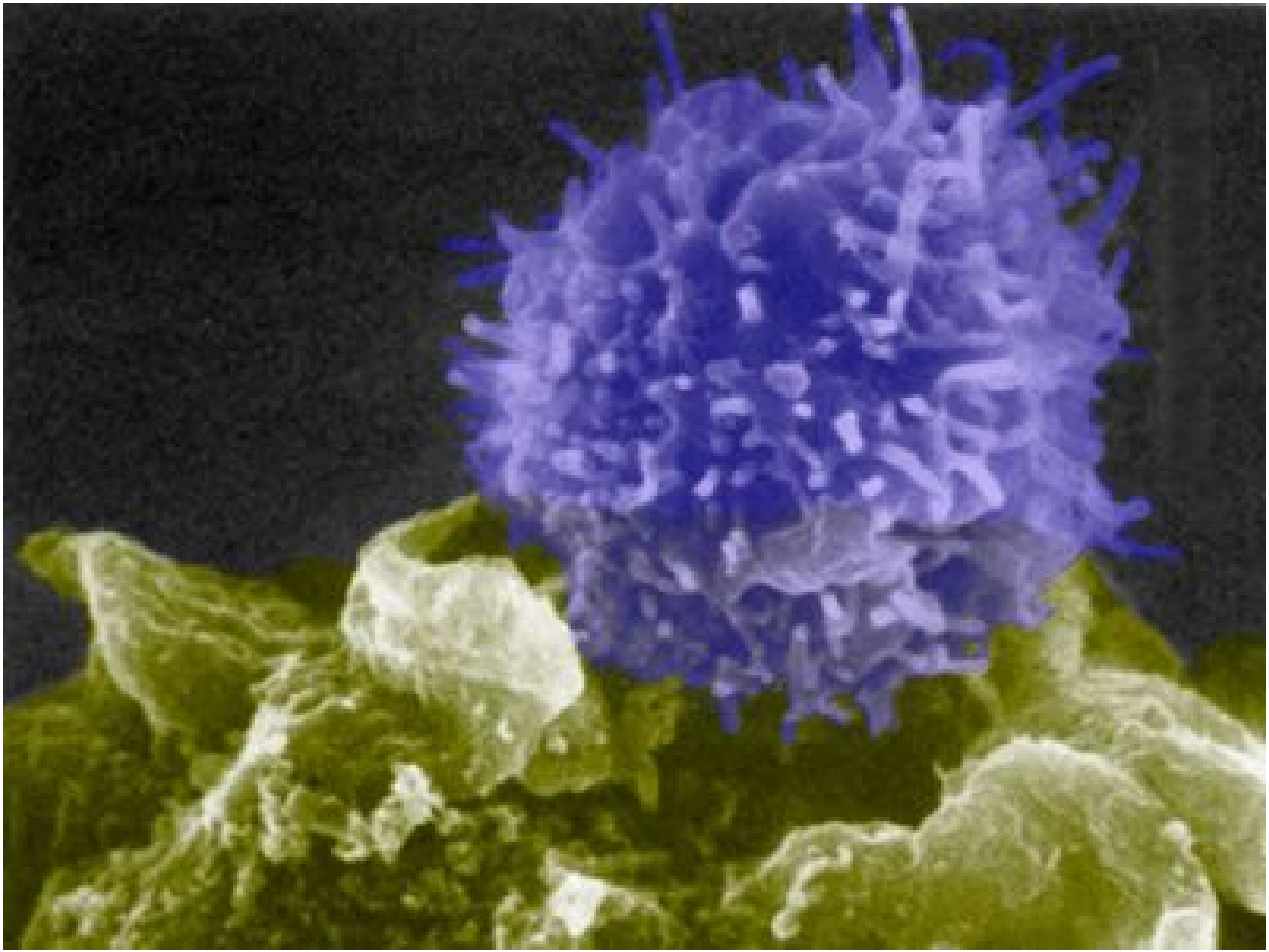
Pathogenesis of Coeliac Disease

- Gliadin is absorbed into the lamina propria and presented in conjunction with HLA-DQ2 or DQ8 cell-surface antigens by antigen-presenting cells, probably dendritic cells, to sensitized T cells expressing the / T-cell receptor. Tissue transglutaminase deamidates gliadin peptides, generating acidic, negatively charged residues of glutamic acid from neutral glutamines (inset). Because negatively charged residues are preferred in positions 4, 6, and 7 of the antigen-binding groove of HLA-DQ2, deamidated gliadin elicits a stronger T-cell response. These lymphocytes then activate other lymphocytes to generate cytokines, such as interferon-, interleukin-4, and tumor necrosis factor (TNF-), which damage the villi, resulting in enteritis. Induction of aberrant HLA class II cell-surface antigens on the enterocytes may permit these cells to present additional antigens to the sensitized lymphocytes.

Pathogenesis of Celiac Sprue

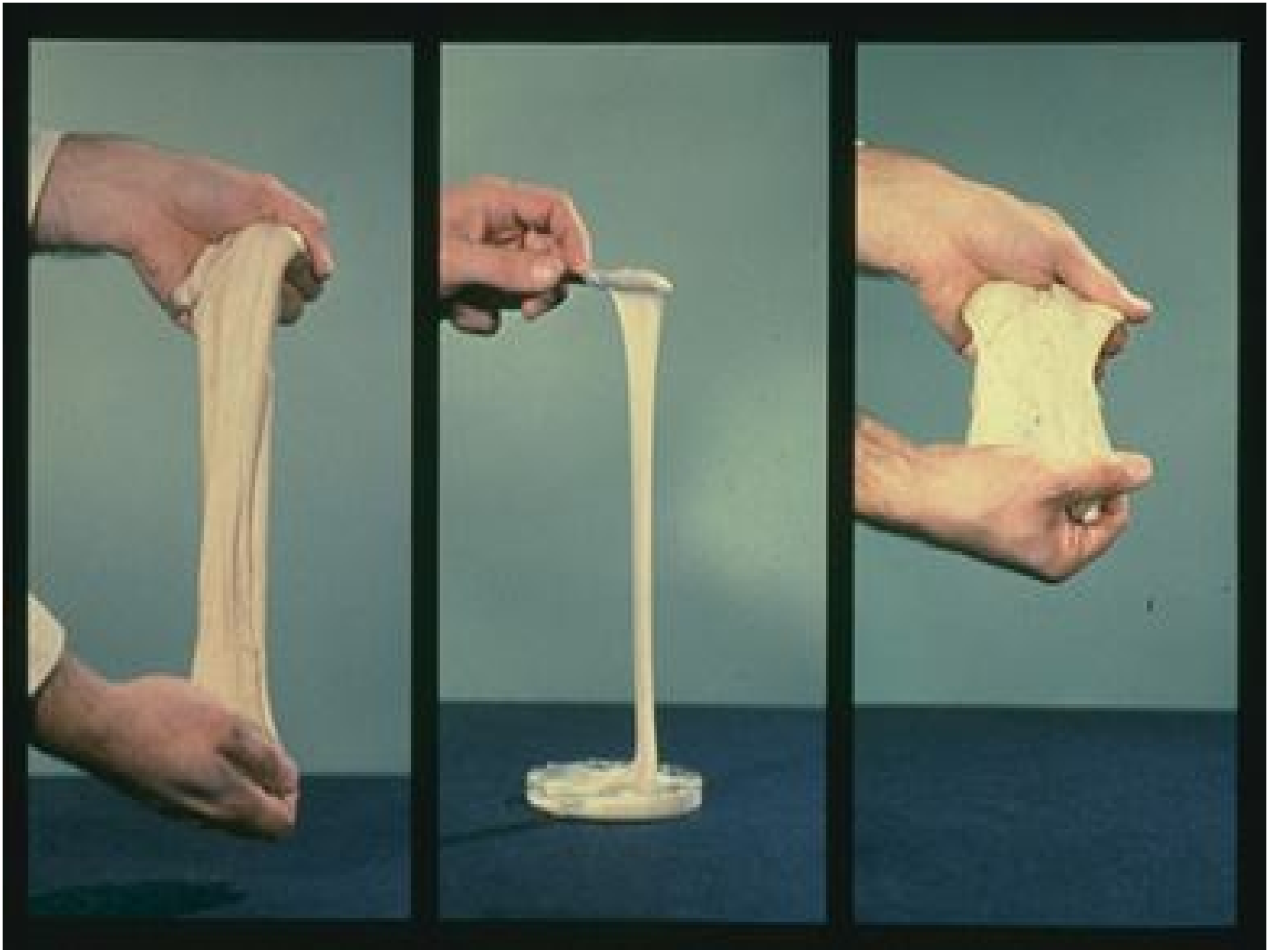


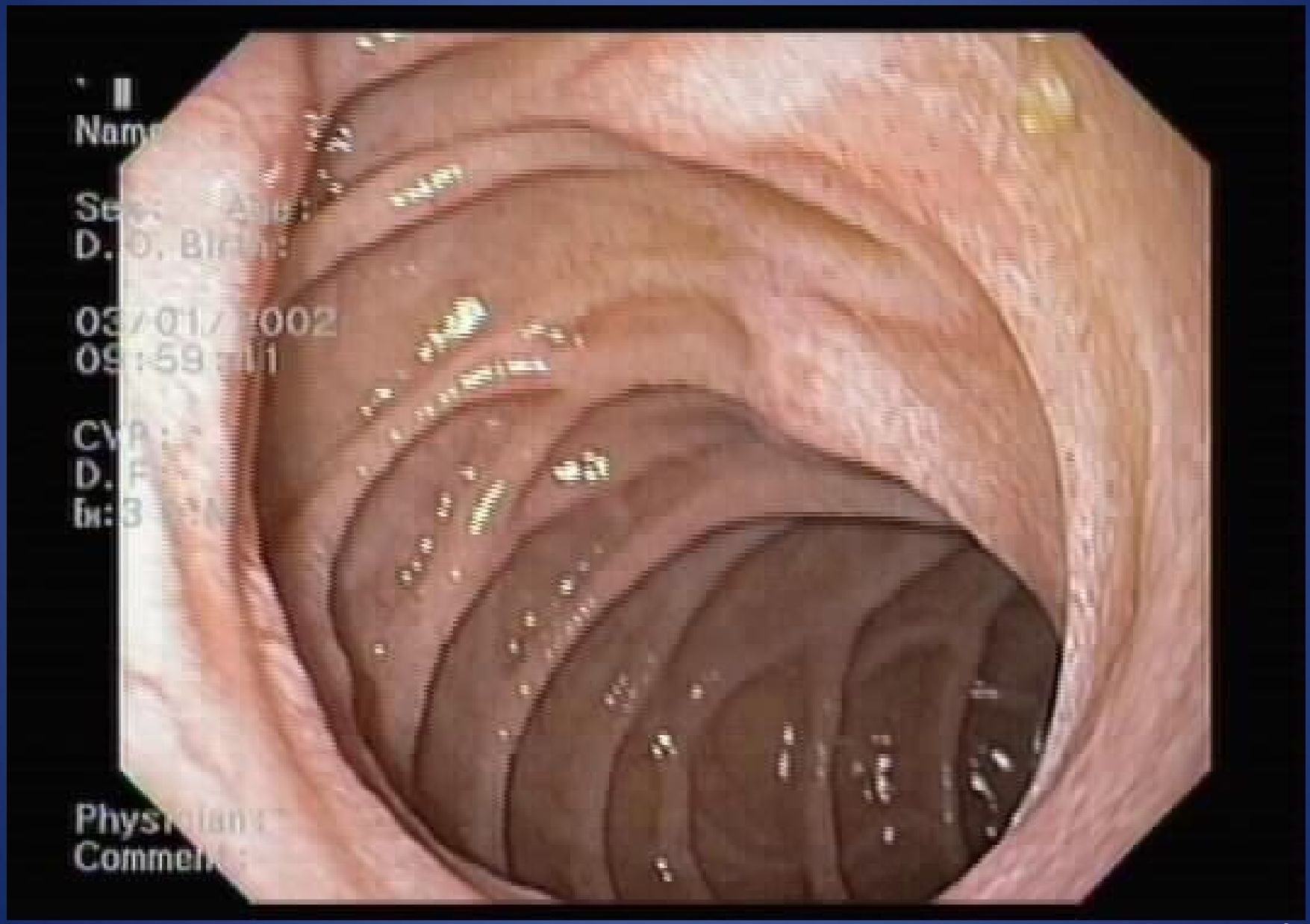
Farrell R and Kelly C. N Engl J Med 2002;346:180-188

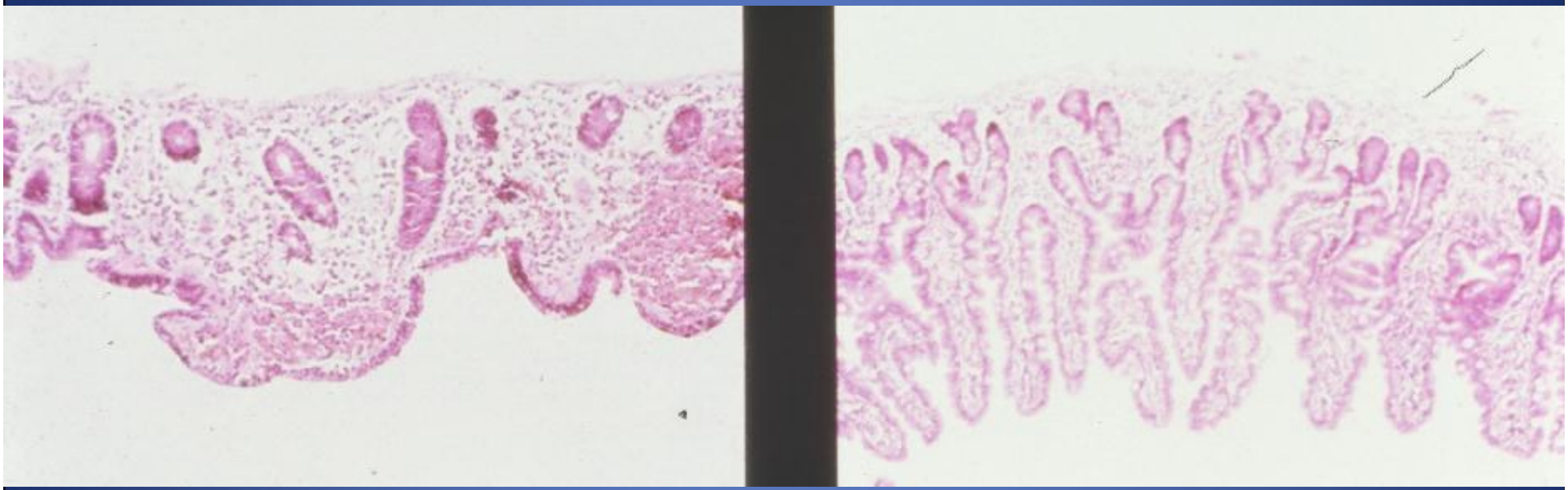


What is coeliac disease?

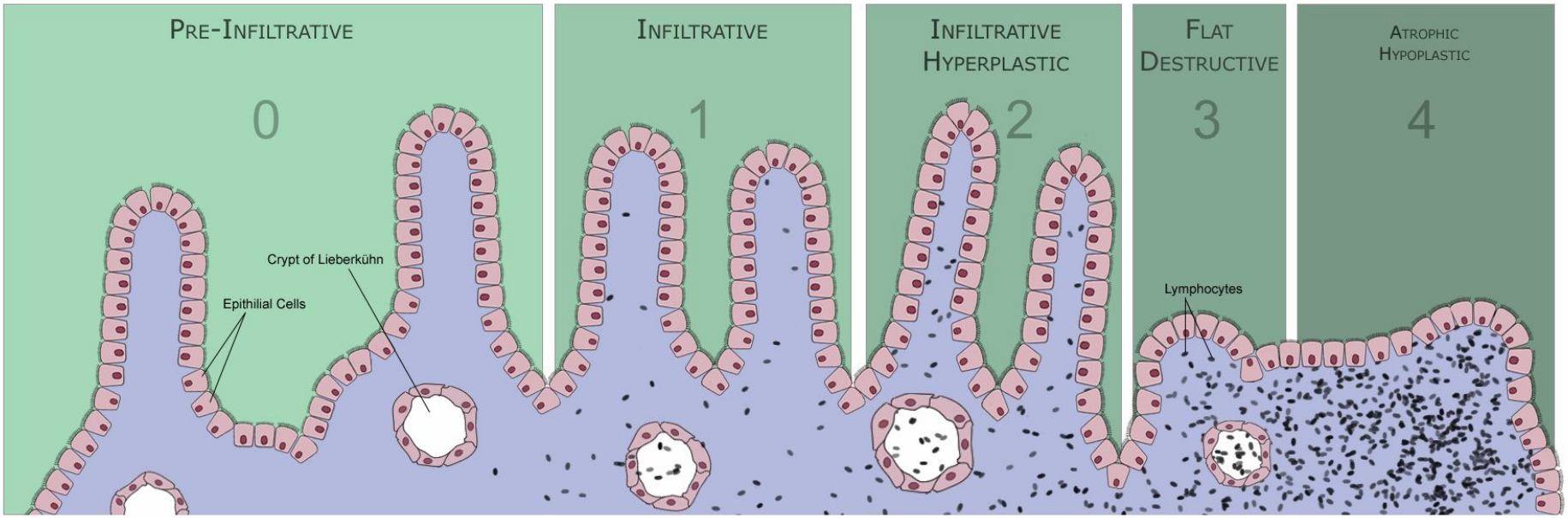
- Provoked by gluten
- T cells are important
- Auto-immune condition
- Some genes make it more likely







Upper Jejunal Mucosal Immunopathology



- PREVALENCE OF COELIAC DISEASE

How many patients do you have?

- Serological population studies suggest prevalence studies 1 in 100-200.
- Estimate currently diagnosed 1 in 420 pts .
- Most GPs 1-4 patients
- Delay in diagnosis 4.5-9 years.

Prevalence of Coeliac Disease

- “1 of every 120 to 300 persons in both Europe and North America.”

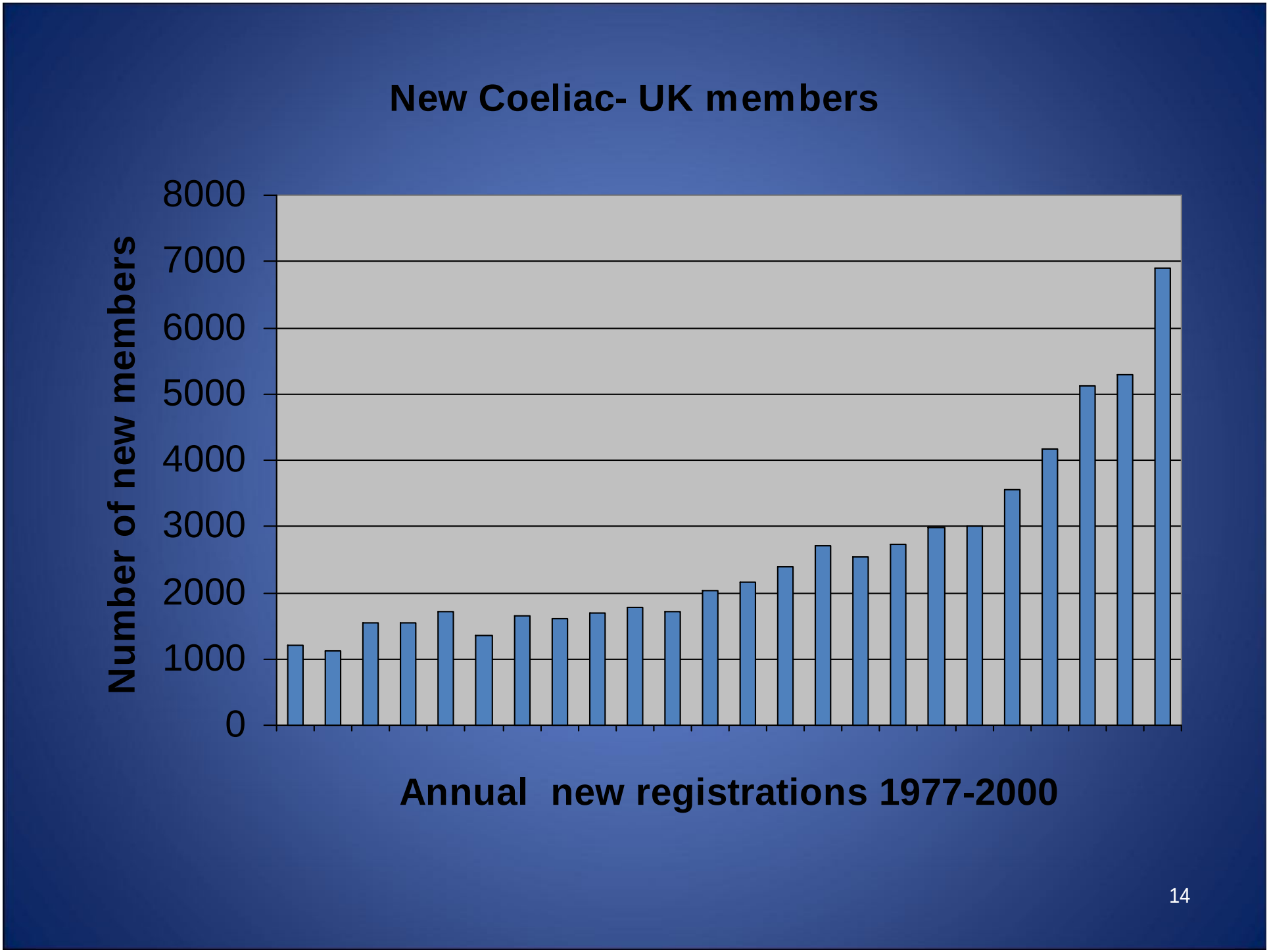
  Farrell and Kelly NEJM 2002

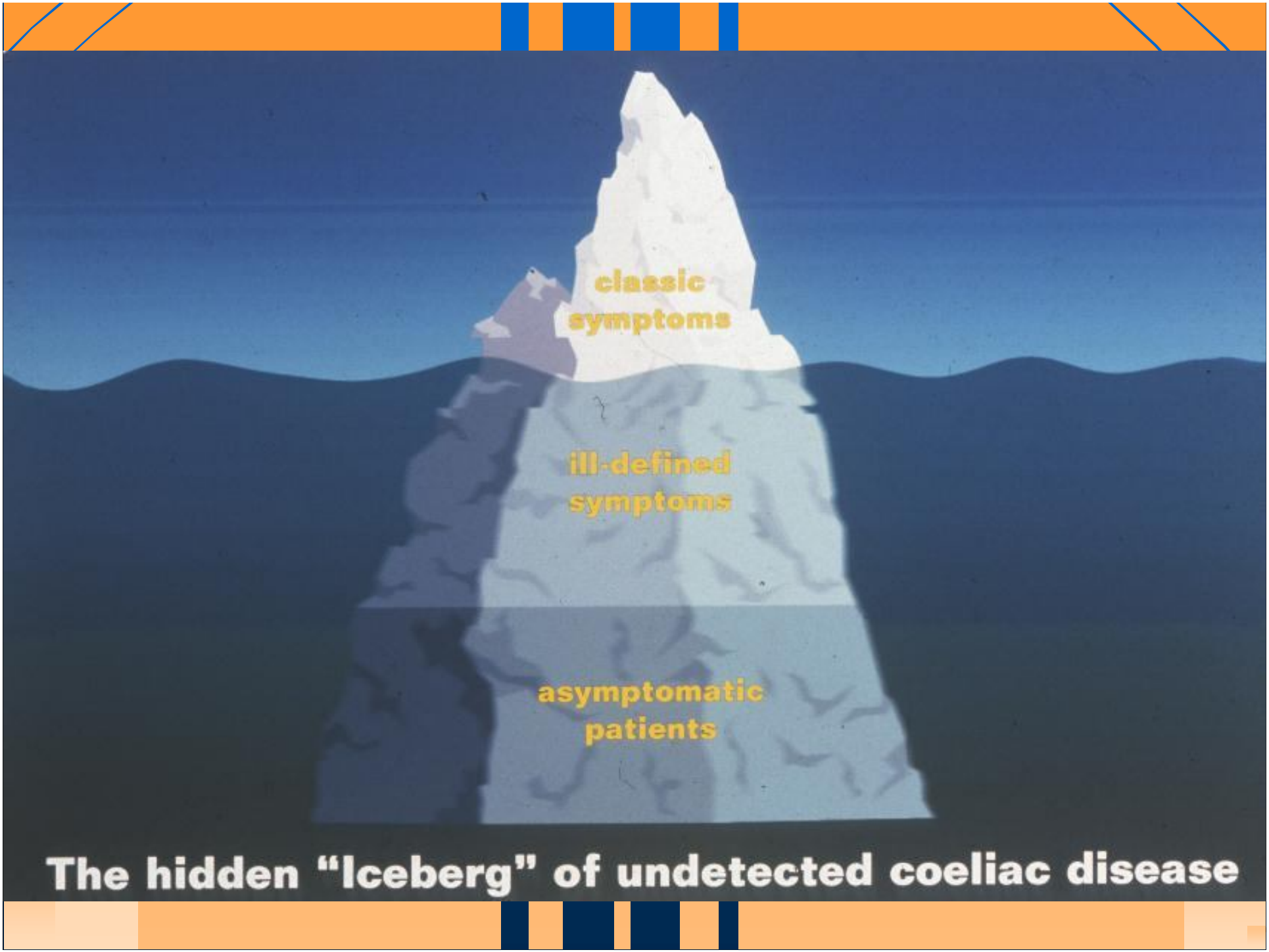
- 1 in 100

  Coeliac UK website

- 11 in 6,200

  Dr Stevens and partners


New Coeliac- UK members
Number of new members
8000
7000
6000
5000
4000
3000
2000
1000
0
Annual new registrations 1977-2000


classic
symptoms
ill-defined
symptoms
asymptomatic
patients
The hidden "Iceberg" of undetected coeliac disease

DISEASE ASSOCIATES OF COELIAC DISEASE

The Spectrum of Clinical Presentations of Celiac Sprue

TABLE 1. THE SPECTRUM OF CLINICAL PRESENTATIONS OF CELIAC SPRUE.

COMMON FEATURES	LESS COMMON FEATURES	ASSOCIATED CONDITIONS	COMPLICATIONS
Adults	General features	Definite associations	Refractory sprue
Iron-deficiency anemia	Short stature	Dermatitis herpetiformis	Enteropathy-associated T-cell lymphoma
Diarrhea	Delayed puberty	IgA deficiency	Carcinoma of the oropharynx, esophagus, and small bowel
Children	Gastrointestinal features	Type 1 diabetes	Ulcerative jejunoileitis
Diarrhea	Recurrent aphthous stomatitis	Autoimmune thyroid disease	Collagenous sprue
Failure to thrive	Recurrent abdominal pain	Sjögren's syndrome	
Abdominal distention	Steatorrhea	Microscopic colitis	
	Extraintestinal features	Rheumatoid arthritis	
	Folate-deficiency anemia	Down's syndrome	
	Osteopenia or osteoporosis	IgA nephropathy	
	Dental-enamel hypoplasia	Possible associations	
	Vitamin K deficiency	Congenital heart disease	
	Hypertransaminasemia	Recurrent pericarditis	
	Thrombocytosis (hyposplenism)	Sarcoidosis	
	Arthralgia or arthropathy	Cystic fibrosis	
	Polyneuropathy	Fibrosing alveolitis	
	Ataxia	Lung cavities	
	Epilepsy (with or without cerebral calcification)	Pulmonary hemosiderosis	
		Inflammatory bowel disease	
	Infertility	Autoimmune hepatitis	
	Recurrent abortions	Primary biliary cirrhosis	
	Anxiety and depression	Addison's disease	
	Follicular keratosis	Systemic lupus erythematosus	
	Alopecia	Vasculitis	
		Polymyositis	
		Myasthenia gravis	
		Schizophrenia	

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Important disease associations for us

- Type 1 Diabetes Mellitus
- Auto-immune thyroid disease
- Osteoporosis
- Iron-deficency anaemia
- Infertility
- Depression/Neuropsychiatric complications
- Hyposplenism
- GI neoplasms

- DIAGNOSIS OF COELIAC DISEASE

How clinicians diagnose coeliac disease

- Blood tests
- Small intestine biopsy
- Improvement on gluten free diet
- Is the biopsy necessary?
- Is a re-challenge and biopsy necessary?
- Why do doctors have different views?

The blood tests

- I gA endomysial antibody
- IgA tissue transglutimanase

Sensitivity and specificty above 90 %

- Be aware of IgA deficiency
- Seronegative coeliac disease 6.4-9.1% of cases.
- In some cases HLA DQ2 and HLA DQ 8 typing may help to make or exclude diagnosis.

The duodenal biopsy

- The gold standard for diagnosis
- Must be on normal diet for 6w before
- Useful if seronegative but strong clinical suspicion.

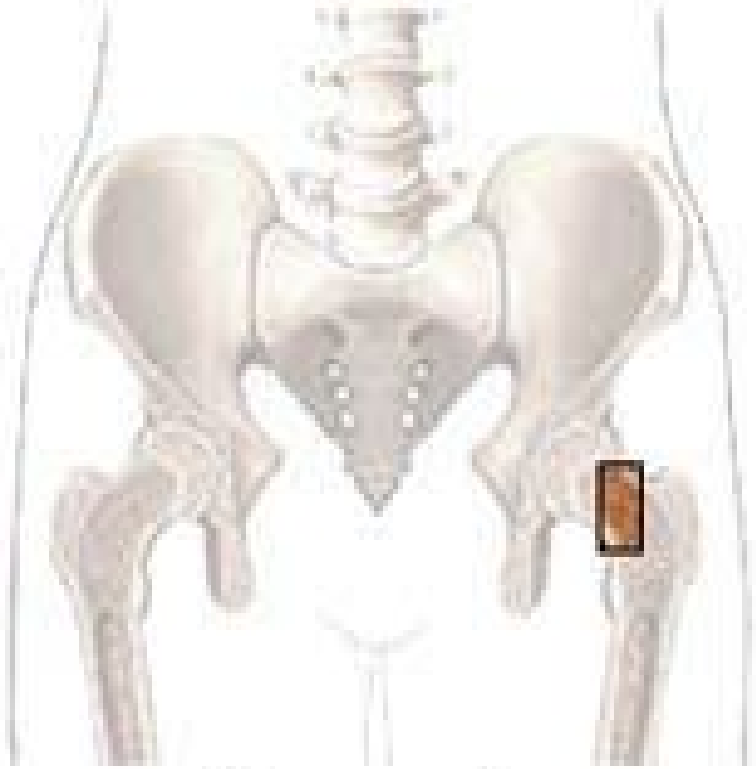
- TREATMENT OF COELIAC DISEASE

Gluten Free Diet

- This diet eliminates all foods that contain wheat, rye, and barley.
- Even small amounts can cause problems.
- It is important not to cross-contaminate these foods.
- Small amount of oats are considered safe .
- Is hard, can be isolating, can get you down.

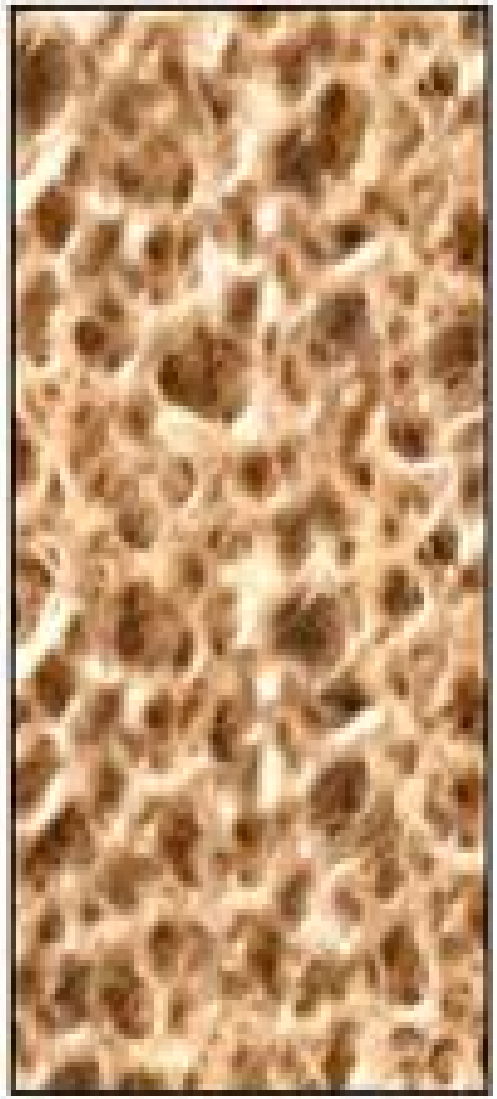
Risks of not keeping to GF diet.

- Effect if small dietary lapses unknown.
- Return of symptoms for some.
- Very small increased risk of small bowel lymphoma, most first year. Risks of breast cancer lower than population [0.35].
- Osteoporosis.
- Fertility problems.

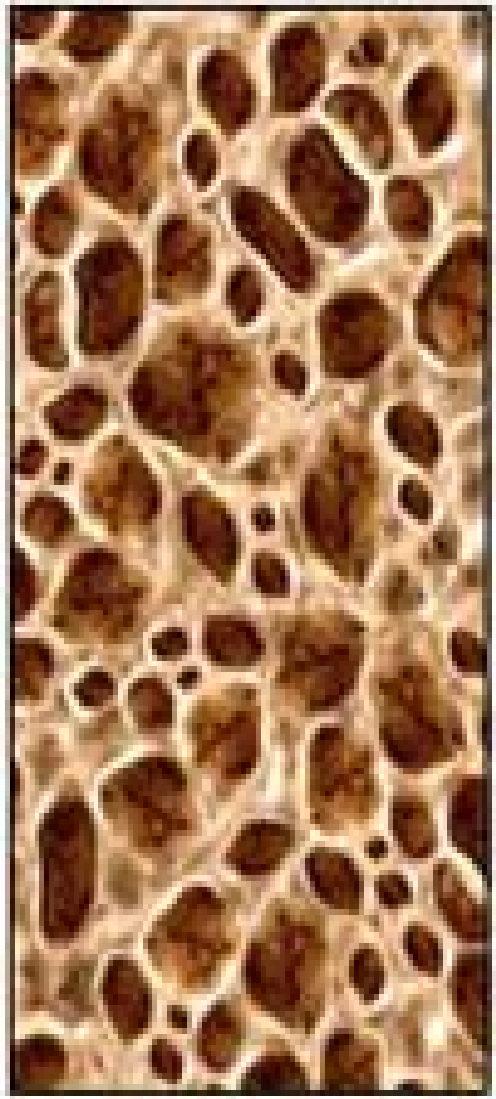


Bone section
through hip

Solid
bone matrix



Weakened
bone matrix



Patient groups with increased prevalence in General Practice

Disease	Estimated frequency
• Dermatitis Herpeteformis	69-89%
• Rec. apthous ulcers	10-18%
• Fe def anaemia	2.7-5.7%
• IBS	0-11.4%
• First degree relatives	4-22%

Questions in Coeliac Disease

- Should we do case finding?
- Should we test relatives of Coeliac patients?
- If so when should we test them? Once only? At intervals? Only when they have symptoms?
- How can you get positive serology test but negative biopsy? What do in these cases?
- AND HOW SHOULD WE LOOK AFTER COELIAC PATIENTS?

AND HOW SHOULD WE LOOK AFTER COELIAC PATIENTS?

- As for any long-term condition with disease and morbidity associates
  - Harm reduction and early diagnosis of complications
  - Support in concordance with the treatment
  - Prescribe and facilitate access to the treatment
  - Form a working therapeutic alliance
  - Deliver care in a structured and patient centred manner